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10/032,393	12/21/2001	Robert Haselbeck	ELITRA.010A	5173

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EXAMINER

VOGEL, NANCY S

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 05/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/032,393

Applicant(s)

HASELBECK ET AL.

Examiner

Nancy T. Vogel

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-135 is/are pending in the application.
- 4a) Of the above claim(s) 12, 23 and 48-135 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11 and 24-47 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 December 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date see office action.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Claims 1-135 are pending in the case.

Receipt of Information Disclosure Statements on 8/1/02, 9/6/02, 10/9/02, 4/22/03 and 3/18/04, is acknowledged.

Election/Restrictions

Claims 12, 23, 41 and 48-135 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the response submitted 3/25/04.

Applicant's election without traverse of Group I, and the species of the promoter of SEQ ID NO:36, the xylO operator, and the Staphylococcus aureus as host, in the response submitted 3/25/04, is acknowledged.

Applicant did not list those claims which are readable on the above elected species, as required in the Office action. Claims 1-11, 13-22, 24-40, 42-47 have been determined to be readable on the elected species and will be examined.

Specification

The disclosure is objected to because of the following informalities: The disclosure is objected to because it contains an embedded hyperlink and/or other form

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of browser-executable code. See page 54 Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Appropriate correction is required.

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 28 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the plasmids recited in this claim are required to practice the claimed invention. Thus, these must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the plasmids. It is not clear that all of the plasmids are

readily available to the public, and thus the plasmids of the claims may not be obtainable without deposit.

Where the invention involves a biological material and words alone cannot sufficiently describe how to make and use the invention in a reproducible manner, access to the biological material may be necessary for the satisfaction of the statutory requirements for patentability under 35 USC 112. Courts have recognized the necessity and desirability of permitting an applicant for a patent to supplement the written disclosure in an application with a deposit of biological material which is essential to meet some requirement of the statute with respect to the claimed invention. *Merck and Col., Inc. v. Chase Chemical Co.*, 273 F. Supp. 68, 155 USPQ 139 (D. N.J. 1967); *In re Argoudelis*, 434 F.2d 666, 168 USPQ 99 (CCPA 1970).

Applicant claims various plasmid constructs in the instant claims. In order to sufficiently enable the claimed plasmids, Applicant must make a biological deposit of each of them. The deposit rules pursuant to 37 CFR 1.801-1.809 set forth examining procedures and conditions of deposit which must be satisfied when a deposit is required. See MPEP 2402-2404.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11, 25, 28-40, 42-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and by dependence claims 2-11, 25, 28-40 and 42-47 are vague and indefinite in its recitation of "said fusion promoter comprising at least one promoter that is modified to have altered activity in at least one gram-positive organism". Claim 1 does not set forth how the promoter is "modified", and what sort of "altered activity" results. The claims could be interpreted as intending that the modification consists of the linkage of the xylO operator to the SEQ ID NO:36 promoter, or alternatively, the modification could be interpreted to be some other, non-specified alteration to the sequence of the SEQ ID NO: 36 and/or the xylO operator. Due to this uncertainty, the intended metes and bounds of the claimed subject matter cannot be determined. Clarification is required. For the purposes of examination, the claims have been examined as if claim 1 recited the fusion promoter consists of SEQ ID NO: 36 which has been modified, wherein the modification consists of operative linkage of SEQ ID NO: 36 to a xylO operator.

Claim 45 is vague and indefinite in the recitation of "a molecule that inhibits the proliferation of microbe". Apparently a word is missing before the word "microbe". In the interest of compact prosecution, the claim has been examined as if it read "a microbe".

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1, 7, 9, and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Marra et al. (WO 99/28508) (cited by applicants).

Marra et al. disclose an isolated nucleic acid comprising a fusion promoter said fusion promoter comprising at least one promoter that is modified to have altered activity in at least one gram-positive organism said promoter being linked to the tet operator (tetO), wherein said at least one operator is positioned such that binding of at least one repressor to said at least one operator represses transcription from said fusion promoter (see page 4 lines 10-19, and page 12, lines 4-20).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 7-11, 13-15, 18-22, 24-27, 29, 32, 33, 36-40, 42-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bujard et al. (EP 0186 069) (cited by applicants) in view of Sizemore et al. (J. Bacteriol. 174 (9): 3042-3048).

Bujard et al. disclose an isolated nucleic acid comprising a fusion promoter comprising the T5 promoter operatively linked to a heterologous operator permitting the control of the promoter activity. The reference discloses that any operator/repressor system may be used (see col. 3-4 and claims). The reference discloses the lacO region linked to the T5 promoter. The fusion promoter is responsive to an inducer (col. 12, example 4). The reference discloses the promoter linked to a reporter gene, contained in a vector, and a host cell comprising the promoter (see Example 4). The difference between the reference and the instant claims is that the xylo operator is linked to the T5 promoter, and the host cell is *S. aureus*.

However, Sizemore et al. disclose nucleic acids comprising the xylose utilization control region for *S. xylosus*, including the operator region (see Fig. 1, and pages 3043-3044, and page 3047, first column). The reference discloses that the control region is induced by xylose. The reference discloses the vectors comprising said nucleic acids, and staphylococcus microorganisms comprising said nucleic acids (see pages 3043-3044).

It would have been obvious to one of ordinary skill in the art to have substituted the xylo operator from a staphylococcus microorganism, for the lacO region in the fusion promoter disclosed by Bujard et al., since both references disclose prokaryotic expression control regions, made up of a promoter and an operator region, and since

Bujard et al. disclose that it is possible to combine the T5 promoter with a heterologous operator, such as that of the lac operon or any other operon, in order to control expression of an operably linked nucleic acid using the native inducer of that operon. One would have been motivated to make the substitution by the known equivalence of functions of the lac and xyl operator regions, and the known usefulness of the xyIO operator region in controlling gene expression, inducible by xylose.

Claims 1-4, 7-11, 13-15, 18-22, 24-29, 32, 33, 36-40, 42-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bujard et al. (EP 0186 069) (cited by applicants) in view of Sizemore et al. (J. Bacteriol. 174 (9): 3042-3048) as applied to claims 1-4, 7-11, 13-15, 18-22, 24-27, 29, 32, 33, 36-40, 42-47 above, and further in view of Shih et al. (US Patent 4,959,311), Kisumi et al (US Patent 4,656,136) or Pederson et al. (Molecular and General Genetics, 244 (4): 374-382 (1994)).

Bujard et al. and Sizemore et al. are cited for the reasons set forth above. The difference between the references and the instant claims is that the vector further comprises a replicon selected from the group consisting of p15a, pC194 and pCT1138. However, Sizemore et al, Kisumi et al., and Pederson et al. disclose respectively, the p15a, pC194 and the pCT1138 replicons and their usefulness in cloning and expression plasmids which are able to replicate in different types of microorganisms. It would have been obvious to one of ordinary skill in the art to have modified any vector disclosed by Bujard et al. in view of Sizemore et al., to comprise a replicon from the p15a, pC194 or pCT1138 replicons disclosed by Shih, Kisumi, or Pederson, since all of the references

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disclose expression vectors which are useful for carrying foreign genes into desired host microorganisms. One would have been motivated to utilize such known replicons in order to take advantage of the known replication properties in the microorganism of interest.

Claims 1-11, 13-27, 29, 32-40, 42-47 rejected under 35 U.S.C. 103(a) as being unpatentable over Bujard (EP 0186 069) in view of Sizemore et al. as applied to claims 1-4, 7-11, 13-15, 18-22, 24-27, 29, 32, 33, 36-40, 42-47 above, and further in view of Bujard et al. (US Patent 5,362,646).

Bujard et al. and Sizemore et al. are applied for the reasons set forth above.

The difference between the references and the instant claims is that two operators are present in the nucleic acid.

However, Bujard et al. disclose nucleic acids which are expression control regions, which comprise a T coliphage promoter linked to an operator region, which may be lacO, and further discloses that two operator regions may be utilized (see col. 5, lines 20 – col. 6, line 5). The reference discloses that high levels of control may be possible using two operator regions (see col. 6, lines 2-3).

It would have been obvious to one of ordinary skill in the art to have inserted two operator regions, as taught by Bujard et al. (US Patent 5,362,646), in the nucleic acids disclosed by Bujard et al. (EP 0186 069) in view of Sizemore, since all of these references disclose the use of heterologous operator regions combined with a strong promoter, to obtain maximum control. One would have been motivated to make the

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addition of a second operator regions by the known benefit of obtaining additional expression control, as disclosed by Bujard et al. (US Patent 5,362,646).

Claims 1-4, 7-11, 13-15, 18-22, 24-27, 29-33, 36-40, 42-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bujard et al. (EP 0186 069) (cited by applicants) in view of Sizemore et al. (J. Bacteriol. 174 (9): 3042-3048) as applied to claims 1-4, 7-11, 13-15, 18-22, 24-27, 29, 32, 33, 36-40, 42-47 above, and further in view of Israelson et al, (Appl. Environ. Microbiol. 61: 2540-2547 (1995)(cited by applicants).

Bujard and Sizemore are cited for the reasons set forth above. The difference between the references and the instant claims is that the reporter gene is lacL-lacM of *Leuconostoc mesenteroides*.

However, Israelson et al. disclose the lacL-lacM reporter gene from *Leuconostoc mesenteroides*, vectors comprising said reporter gene, and cells comprising said vectors. Israelson et al. disclose that said reporter genes are useful for evaluating nucleic acid regions for their promoter strength (see abstract and page 2546, first column). It would have been obvious to one of ordinary skill in the art to have utilized the known lacL-lacM reporter gene of Israelson et al., in the vectors disclosed by Bujard in view of Sizemore, since Bujard and Sizemore disclose a promoter/operator region useful for expression of heterologous genes, and since Israelson et al. disclose reporter genes useful for the isolation and evaluation of promoters of interest. One would have been motivated to use the reporter genes of Israelson et al. operatively linked to the promoter/operator disclosed by Bujard and Sizemore, in order to obtain

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information regarding the level of expression of the promoter region. The use of reporter genes is well known and routine in the art.

Conclusion

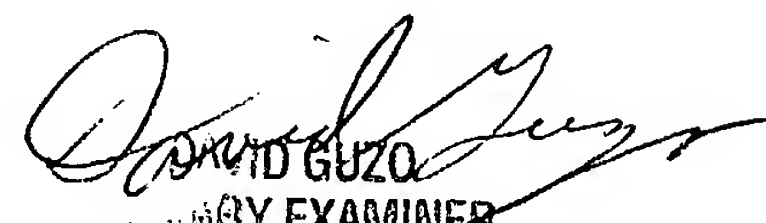
No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy T. Vogel whose telephone number is (571) 272-0780. The examiner can normally be reached on 6:30 - 3:00, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

5/11/04


DAVID GUZO
PRIMARY EXAMINER